PAPER

Vertebrobasilar dolichoectasia diagnosed by magnetic resonance angiography and risk of stroke and death: a cohort study

E E Ubogu, O O Zaidat

....

Objective: There are only limited epidemiological studies evaluating the association between vertebrobasilar dolichoectasia (VBD) and outcomes. This study was designed to elucidate the outcome and prognosis of adults diagnosed with VBD by magnetic resonance angiography (MRA) and to ascertain if these outcomes were independent of known vascular risk factors.

Methods: A cohort study was designed to compare VBD cases identified retrospectively from a computerised database of MRA reports with age and sex matched controls evaluated after a 4–7 year period, and 1440 MRA reports were reviewed. The inclusion criteria were age $\geqslant 18$ years and a radiological diagnosis of VBD. Patients were excluded if there was haemodynamically significant stenosis or occlusion of the posterior circulation. Data were obtained by medical record review and telephone questionnaires. The primary outcome measure was transient or fixed posterior circulation dysfunction (PCD), with a secondary outcome measure of all cause mortality.

Results: Sixty four VBD cases were obtained, and 19 cases (30%) were excluded due to refusal and/or insufficient follow up data. From the same computerised database, 45 controls were selected by consecutive sampling. The mean age at follow up was 73.4 years for VBD cases and 73.1 years for controls, with a median follow up period of 64 months. VBD was associated with fixed/transient PCD ($p = 0.0001$; estimated adjusted odds ratio (OR) of 20.6 and confidence interval (CI) of 4.4 to 95.3), and with all cause mortality (OR = 3.6 CI 1.3 to 10.3); ($p = 0.018$). VBD cases had 36% mortality, with 50% occurring within 34 months of the initial diagnosis. The VBD cumulative survival curve was statistically different from the controls ($p = 0.012$ by Mantel-Cox log rank test).

Conclusions: This study suggests that VBD may be an independent risk factor for stroke. VBD cases had an increased likelihood for PCD, all cause mortality, and reduced cumulative survival independent of other vascular risk factors in this cohort. Larger population based prospective studies are required to verify these results.

See end of article for authors' affiliations
....

Correspondence to:
Dr O O Zaidat,
Department of Radiology,
Duke University Medical
Center, Box 3808,
Durham, NC 27560, USA;
ozaidat@hotmail.com

Vertebrobasilar dolichoectasia (VBD) is an uncommon vasculopathy of unclear aetiology affecting the arterial wall of vertebral and/or basilar arteries.[1] This disease causes arterial elongation and enlargement, with subsequent haemodynamic and hemostatic changes leading to thrombosis, micro-embolisation, and brainstem compression, with or without aneurysm formation.[1] A variety of clinical syndromes have been associated with ectatic vertebrobasilar arteries. These include an assortment of isolated or combined brainstem/cranial nerve syndromes,[2–8] cervicomedullary junction compression,[2 6 9–13] transient or permanent motor deficits,[6 8 10 12 14 15] cerebellar dysfunction,[10] central sleep apnoea,[16] hydrocephalus, and ischaemic stroke.[8 12]

These presentations may be due to ischaemic infarction in the arterial distribution of these vessels or local compression.[1 2 4 6 8–11 14] It is unclear if VBD may be independently associated with poor outcomes. There are very limited published epidemiological data evaluating VBD and its associations. The purpose of this study was to elucidate whether VBD is independently associated with posterior circulation dysfunction (PCD) irrespective of other vascular comorbidities, and to decipher if this entity may be associated with reduced survival compared with a control group.

METHODS

Patients were retrospectively selected by reviewing computerised records of all intra- and extra-cranial magnetic resonance angiograms (MRA) and the accompanying magnetic resonance images (MRI) of the brain performed at University Hospital between 1 January and 31 December 1995, 1997. The MRA were obtained using a 1.5 Tesla whole body magnet scanner (Magnetom Vision; Siemens Medical System, Erlangen, Germany) with 3 dimensional time of flight (TOF) images with a field of view of 200 mm enhanced by maximum intensity projection techniques, using the following specifications. Intracranial MRA: repetition time (TR) = 32 ms, echo time (TE) = 6 ms, effective slice thickness = 1 mm, data matrix = 144×256, pixel size = 1.04×0.78 mm, measurement time ~10 minutes, number of acquisitions = 1, with vessel contrast enhancement using magnetisation transfer saturation pulse. Extracranial MRA: TR = 30 ms, TE = 6 ms, effective slice thickness = 1.3 mm, data matrix = 163×256, pixel size = 0.92×0.78 mm, measurement time ~8 minutes, number of acquisitions = 1. The 3 dimensional TOF intracranial and extracranial MRA were performed without intravenous gadolinium contrast administration.

....

Abbreviations: BA, basilar artery; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging/images; PCD, posterior circulation dysfunction; TOF, time of flight; VA, vertebral arteries; VBD, vertebrobasilar dolichoectasia

The MRI images in the axial, coronal and sagittal planes were obtained with a 230 mm field of view with slice thickness of 5 mm and interslice interval of 0.40 mm, using standard spin echo T_1 (TE = 450 ms, TR = 12 ms, data matrix = 159×256, pixel size = 1.08×0.90 mm, number of acquisitions = 2), turbo spin T_2 (TE = 3500 ms, TR = 96 ms, data matrix = 154×256, pixel size = 1.12×0.90 mm, number of acquisitions = 1) and fluid attenuated inversion recovery (TE = 9000 ms, TR = 110 ms, TI = 2500 ms, data matrix = 154×256, pixel size = 1.12×0.90 mm, number of acquisitions = 1). VBD was diagnosed by board certified neuroradiologists, applying the computed tomography (CT) criteria of Smoker et al[17] and MRI criteria of Giang et al,[18] as MRA criteria have not yet been established. The arterial dimensions were subsequently measured directly on hard copies using a 4 dioptre handheld lens, calipers, and a pre-adjusted millimetre scale provided for the MRA images corrected for minification.

Based on the above methods and criteria, ectasia of the vertebrobasilar system was defined as arterial diameter >4.5 mm in any location along its course. For the basilar artery (BA), bifurcation above the suprasellar cistern or evidence of any portion lateral to the margin of the clivus or dorsum sellae was considered elongated.[17] [18] Measurements on the MRA source images using the above neuroanatomical landmarks, prior to 3 dimensional TOF arterial reconstruction and direct MRA measurements, revealed that a length >29.5 mm or lateral deviation >10 mm perpendicular to a straight line joining the BA origin to its bifurcation on MRA was abnormal. As there are no established data for the intracranial vertebral arteries (VA), any portion of the VA or origin of the BA above the level of the pontomedullary junction was considered elongated. Using the aforementioned technique, VA on intracranial MRA were considered elongated if the length was >23.5 mm. Any portion of the VA with deviation >10 mm perpendicular to a straight line joining its intracranial entry point to the BA origin was considered abnormal for the purposes of this study. The institutional review board at University Hospital approved the study, and consent was waived for chart review. Verbal consent was considered sufficient for the telephone interview. The investigators conducted the chart review and the telephone interviews.

Selection criteria

Patients were included if they were aged 18 years or older on the date of the initial MRA and there was a radiological diagnosis of dolichoectasia affecting any part of the extra- or intra-cranial vertebrobasilar system as outlined above. The initial MRA had to have been performed between 1995 and 1997. The earliest MRA obtained within the study period was considered to be the initial scan for the purposes of this study. Patients were excluded if they had evidence of haemodynamically moderate (50–70%) to severe stenosis (>70%) or occlusion of the posterior circulation on the initial MRA, as outcomes could be attributable to pre-existing atherosclerotic arterial disease. The radiological data obtained from the computerised MRA database included the reason for study and contained detailed anatomical descriptions of the vasculature by the interpreting neuroradiologists.

A telephone interview questionnaire was designed to obtain additional data to supplement and verify the medical records, as well as follow up outcome events data. Follow up was timed as the interval between patient contact and the initial scan. The next of kin was contacted for patients who had died. In these cases, the follow up period was timed as the interval between the initial MRA and death. Details of the circumstances and causes of death were obtained from the contact individuals and medical records. Data collection

started only after all cases of VBD were identified from the computerised records. Approximate age and sex matched controls with normal MRA scans were obtained from the same cohort within that period by consecutive sampling. If there was patient refusal or incomplete data, the next matched control was selected until there were an equal number of controls for the VBD cases. An age variation of ±5 years and a gender variation of <5% were considered adequate matching between cases and controls. The clinical histories and the baseline medical conditions of the cohort were unknown to the investigators prior to data collection. Official medical records were obtained and reviewed to confirm the data obtained by the telephone questionnaire in all cases, and in a few cases, further information was obtained from the primary care physicians with patient approval.

Outcome measures

The primary outcome measure was the development of transient or fixed neurological deficit in the posterior circulation; posterior circulation dysfunction (PCD), as determined by a board certified neurologist who was not involved in the initial data collection or review of computerised MRA records. The secondary outcome measure was all cause mortality.

Statistical analysis

Demographic and clinical variables were dichotomised, producing 2×2 contingency tables, and analysed for differences between the cases and controls by Fisher's exact test. Logistic regression analysis was used for the analysis of association between VBD and the outcome measures, with level of significance set at $p<0.05$. Odds ratio (OR) was calculated for any significant associations with adjustment for possible confounding factors, with 95% confidence intervals (95% CI). The Kaplan-Meier cumulative survival curve was computed with significance between the cases and controls calculated with a log rank test (Mantel-Cox) with significance set at $p<0.05$. The data were analysed using Statview® (version 6.0; SAS, Cory, NC, USA)

RESULTS

A total of 1440 MRA reports was reviewed, revealing 64 patients with VBD without any evidence of significant stenosis or occlusion in the posterior circulation. The mean age of the MRA cohort was 67.6 years (range 18–97). This resulted in a VBD prevalence of 4.4% (4400 in 100 000) in this tertiary referral hospital based cohort. Nineteen patients were excluded due to refusal to participate, or the presence of inadequate, incomplete, or conflicting follow up data. The 45 cases available for the final analysis were compared with 45 age and sex matched controls from the same cohort. Twenty six VBD cases (58%) were symptomatic on presentation, while 19 cases (42%) had incidental VBD findings on MRA performed for various indications other than PCD, including headache, aneurysm, neoplasm, and anterior circulation stroke/transient ischaemic attacks. The mean (SD) age at follow up was 73.4 (12.5) years for the case group and 73.1(12.2) years for the control group, with a total median follow up period of 64 months (range 1–78).

VBD was more common in women (32/45) and was equally distributed between whites (22/45) and African-Americans (23/45) in the case group. Hypertension was present in 32 cases (71%), with diabetes mellitus occurring in eight cases (18%). Hyperlipidaemia and coronary artery disease were present in 14 (31%) and 13 (29%) cases respectively. Thirteen cases with VBD had coronary artery disease in contrast to five patients in the control group (p = 0.063), while peripheral vascular disease was more common in the VBD group (11 v 5,

p = 0.167). The use of aspirin for stroke prophylaxis between the initial MRA and follow up was present in 26 cases (58%), while warfarin was used in 13 cases (29%). There were no VBD cases on clopidrogel prophylaxis during the study period. Five control patients were on this anti-platelet agent, but this was not statistically significant (p = 0.056). There was clinical evidence of previous posterior circulation strokes in seven patients with VBD but only one patient in the control group (p = 0.058). Prior posterior circulation transient ischaemic attacks were more common in VBD cases than controls, but this was not statistically significant (5 v 0, p = 0.056). Comparisons between the cases and control groups in terms of clinical and demographic features are shown in table 1.

BA involvement in VBD was present in 27 cases (60%). MRA evidence of concomitant atherosclerotic disease (defined as >25% stenosis) involving the posterior circulation was absent in 37 VBD cases (82%). There were 6 cases (13%) of anterior circulation atherosclerosis in the VBD case group compared with 10 (22%) control cases (p = 0.20). There was evidence of initial infarct on MRI in 31 VBD cases (69%) and 22 controls (49%). There was no statistically significant difference between the groups (p = 0.07). There were 27/31 cases with anterior circulation infarcts and 20/31 cases with prior posterior circulation infarcts on the initial MRI in the VBD group. This is in contrast to 21/22 with prior anterior circulation infarcts and 13/22 with prior posterior circulation infarcts in the controls. Lacunar infarcts, defined as an irregularly margined hypointense T_1 with corresponding hyperintense T_2 signal <15 mm diameter on MRI, were diagnosed on the initial MRI in 88% and 76% of anterior circulation (p = 0.07) and 70% and 67% of posterior circulation infarcts (p = 0.11) in the VBD case and control groups respectively. Evidence of brainstem compression, defined as MRI evidence of distortion of the normal contour of the midbrain, pons, or medulla, was found in five VBD cases (11%) on initial MRI. Radiological findings are summarised in table 2.

Using univariate analysis, there was no statistically significant difference between case and control groups in terms of demographic or clinical features. In the VBD group, there were 22 cases of PCD (transient = 6, fixed = 16),

Table 1 Demographic and clinical features of VBD cases and controls

Variable	Cases	Controls	p value
Mean age, years (SD)	73.4 (12.5)	73.1 (12.2)	
Age range (years)	49–94	49–93	
Male sex	15 (33%)	13 (29%)	
African-American	23 (51%)	18 (40%)	
White	22 (49%)	25 (56%)	
Other ethnic groups	0 (0%)	(4%)	
Hypertension	32 (71%)	29 (64%)	
Diabetes mellitus	8 (18%)	4 (9%)	
Hyperlipidaemia	14 (31%)	12 (27%)	
Atrial fibrillation	6 (13%)	5 (11%)	
History of smoking	21 (47%)	18 (40%)	
History of alcohol use	8 (18%)	9 (20%)	
Coronary artery disease	13 (29%)	5 (11%)	0.063
Peripheral vascular disease	11 (24%)	5 (11%)	0.167
Hypercoagulable state	3 (7%)	1 (2%)	
Previous aspirin use	26 (58%)	26 (58%)	
Previous clopidrogel use	0 (0%)	5 (11%)	0.056
Previous warfarin use	13 (29%)	10 (22%)	
Previous anterior stroke	8 (18%)	8 (18%)	
Previous anterior TIA	5 (11%)	5 (11%)	
Previous posterior stroke	7 (16%)	1 (2%)	0.058
Previous posterior TIA	5 (11%)	0 (0%)	0.056

TIA, transient ischaemic attack.

Table 2 Radiological characteristics of the VBD case group

Radiological findings	Number of patients (%)
VBD location: basilar artery alone	18 (40%)
Bilateral vertebral arteries	10 (22%)
Basilar artery and both vertebrals	7 (16%)
Unilateral vertebral artery	8 (18%)
Basilar artery and single vertebral	2 (4%)
Concomitant posterior circulation atherosclerosis	
Absent	37 (82%)
Distal to dolichoectasia	5 (11%)
Proximal to dolichoectasia	2 (4%)
Proximal and distal to dolichoectasia	1 (2%)
Anterior circulation atherosclerosis	6 (13%)‡
Infarct on initial MRI	
Present (all locations)	31 (69%)
Anterior circulation infarcts	27 (60%)†§
Posterior circulation infarcts	20 (44%)†¶
Absent	14 (31%)
Brainstem compression on initial MRI	
Present	5 (11%)
Absent	40 (89%)

†Percentages add up to >100% due to dual circulation infarct locations in 16 VBD patients on initial MRI; ‡ 10 (22%) in control group (p=0.20), §v 21 (47%) in control group (p=0.15), ¶v 13 (29%) in control group (p=0.06).

compared with two cases in the control group (both fixed). VBD was statistically significantly associated with the primary outcome, transient/fixed PCD (p = 0.0001, estimated adjusted OR = 20.6, 95% CI 4.4 to 95.3), and all cause mortality (p = 0.018, OR = 3.6, 95% CI 1.3 to 10.3). The median time to primary outcome was 27 months in the case group with a median time to death of 37 months (50 months in the controls). There were 16 deaths (36% mortality) in the VBD case group, with 50% of the mortality occurring within 34 months of the diagnosis. In contrast, there were six deaths (13% mortality) in the control group. The causes of death were variable among the cases and are summarised in table 3. The Kaplan-Meier cumulative survival curve was statistically significantly different between cases and controls (p = 0.012), as shown in fig 1.

DISCUSSION

This retrospective cohort study is the only long term epidemiological study known to the authors that specifically looks at the clinical outcomes and prognosis of VBD compared with a control group. In a small case series without a control group, the actuarial survival rate in VBD after 3 years' follow up was found to be 60%.[12] Another study of intracranial dolichoectasia suggested reduced mean and peak transcranial Doppler flow velocities compared with an age adjusted control group and suggested an increased prevalence of stroke in this cohort.[19]

VBD is a potentially severe condition that may cause severe disability due to ischaemic or compressive dysfunction in the posterior fossa. This may be a condition that is not readily recognised by neurologists or radiologists owing to the "normal" variation in the tortuosity or calibre of the vertebral and basilar arteries in healthy individuals. The radiological diagnosis used in this study was based on a semi-quantitative assessment with extrapolation from CT and MRI criteria for the BA,[17 18] as there are no defined criteria for distal vertebral arteries or MRA criteria for the diagnosis of VBD. This may result in a reduced inter-rater reliability in the radiological diagnosis using MRA. There may be potential for the under- or over-diagnosis of this disease, depending on the presence of PCD on clinical presentation, with or without concomitant atherosclerotic disease of the vertebrobasilar circulation. The

**Table 3** Causes of mortality in the VBD case group

Causes of death	Number of cases† (%)
Respiratory failure	6 (37.5%)
Bronchopneumonia	2 (12.5%)
Pontomedullary stroke	1 (6.3%)
Interstitial pneumonitis	1 (6.3%)
Pulmonary embolism	1 (6.3%)
Post-operative anesthesia	1 (6.3%)
Cardiac arrest with anoxic brain injury	5 (31.3%)
Ventricular fibrillation	2 (12.5%)
Ventricular tachycardia	2 (12.5%)
Pulseless electrical activity	1 (6.3%)
Ischaemic stroke	2 (12.5%)
Pontomedullary stroke	1 (6.3%)
Right cerebellar stroke	1 (6.3%)
Intracranial haemorrhage	2 (12.5%)
Right frontoparietal intraparenchymal bleed	1 (6.3%)
Subarachnoid bleed: BA aneurysm rupture	1 (6.3%)
Brainstem compression	2 (12.5%)
Right cerebellar stroke	1 (6.3%)
BA aneurysm with pontine compression	1 (6.3%)
Myocardial infarction	1 (6.3%)
Necrotizing pancreatitis	1 (6.3%)
Colon cancer	1 (6.3%)
Aortic aneurysm rupture	1 (6.3%)

†Percentages add up to >100% due to several attributable causes of death in this group.

Figure 1 Kaplan-Meier curve showing the cumulative survival among VBD cases compared with controls over time.

clinical diagnosis of symptomatic VBD should be made based on PCD in the absence of significant stenotic or occlusive disease of the posterior circulation with ectatic and tortuous vessels present on angiography, and of any other potential causes for the symptoms. Asymptomatic VBD should be diagnosed by the presence of dolichoectatic vessels in the absence of any symptoms referable to the posterior circulation.

MRA has not been directly compared with contrast angiography techniques in recognizing VBD, so its sensitivity and specificity are unknown. However, this is an acceptable method for identification, and reduces the morbidity associated with an invasive procedure.[17 19] Our study uses a single radiological technique for diagnosis, avoiding possible methodological flaws seen in previous smaller studies.[12 19–21] The severity of VBD was not uniformly documented in this study, as published CT/MRI criteria require anatomical boundaries that are routinely eliminated by the maximum intensity projection techniques used in acquiring three dimensional TOF MRA images. The utilisation of abnormal flow voids on MRI may provide some information on severity, but fails to give the entire picture of the vasculature involved. The degree of atherosclerosis can be determined from MRA by subtracting the luminal diameter of the most stenotic portion of the artery from the proximal normal vessel diameter and multiplying the ratio of this difference to the normal diameter by 100%, as established with contrast angiography.[22]

The prevalence in VBD in this cohort may be higher than in the general population, as cohorts obtained from hospital based databases are usually older, as shown in this study, and are more likely to have pathology (selection and referral bias). The prevalence in this cohort is similar to that published from a cohort of 385 people presenting with their first ischaemic stroke in Rochester, MN, USA between 1985 and 1989 (4.4% v 3.1%).[20] However, that study included all cases of intracranial dolichoectasia in a symptomatic stroke population, and the diagnostic capabilities for VBD on the available MRI scanners at the time may have been reduced compared with more modern scanners. The overall low prevalence rate reported in the literature may be related to an
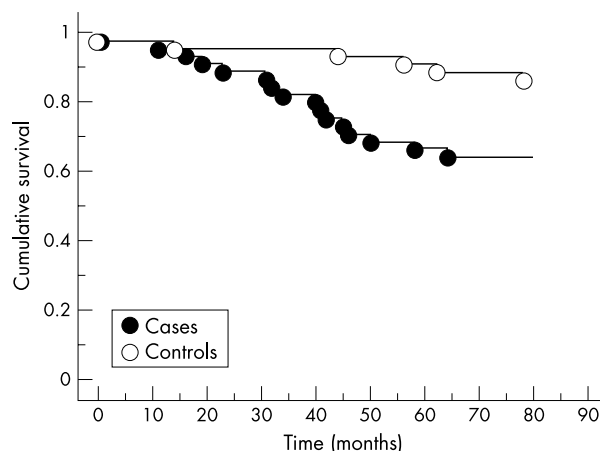
increased potential for under-diagnosis of VBD or the lack of verified and uniformly accepted angiographic criteria. This paper emphasises the need for strict criteria for identifying VBD angiographically.

The strong statistical association between the presence of VBD as diagnosed on MRA, PCD and all cause mortality is consistent with previously published literature despite study limitations. The small sample size with consequential reduced study power could result in non-statistically significant, but clinically relevant associations. The further loss of 19 cases caused by patient refusal and incomplete data may have inaccurately skewed results. Retrospective data collection has empirical flaws, as patients with disease are more likely to recall subsequent illness, and there is potential ascertainment bias by the data collector. In this cohort, the VBD cases were rarely aware of that diagnoses because the arterial changes were believed to be benign and insignificant by the treating physicians. Despite these difficulties, this study is the largest epidemiological study of VBD diagnosed by a single radiological modality at a single institution with significant long term follow up.

This cohort study suggests that VBD (defined as BA or VA diameter >4.5 mm or deviation of any portion >10 mm from the shortest expected course, BA length >29.5 mm or intracranial VA length >23.5 mm) may be an independent risk factor for fixed or transient PCD and all cause mortality in this cohort. The presence of traditional stroke risk factors was distributed evenly among cases and controls. These results would suggest that VBD may be a congenital vasculopathy of the elastic layer of the arterial wall, and may cause PCD independent of atherosclerotic disease affecting the intimal layer.[13 21] The reduction in cumulative survival with time suggests that patients with VBD have higher mortality rates than an age and sex matched cohort. The association of VBD with all cause mortality could be secondary to ischaemic or compressive PCD or may indicate that VBD is part of a more widespread vasculopathy.[21]

The factors that may result in the pathological presentation of VBD remain unclear. Upper cervical spinal/neck trauma or severe systemic hypertension with consequential arterial dissection,[2 20 21] VBD induced aneurysmal formation and rupture,[12 21 23 24] or brainstem compression due to worsening vessel enlargement and tortuosity are potential mechanisms.[2 6 9–12 19 21] Recurrent thromboses may occur due to turbulent blood flow, resulting in vessel stenosis or occlusion. Thrombus with local or distal micro-embolisation may also be an important pathogenic mechanism for ischaemic strokes.[1 20 21 24] Transient hypotension in a maximally com-

pensated and autoregulated posterior circulation with abnormal flow can be hypothesised as an unproven but potential mechanism for clinical presentation in VBD. Another hypothesis that may explain posterior circulation ischaemia could be related to induced atherosclerosis[20][21] in dolichoectatic arteries at the regions of maximum angulation, although histological studies show defects in the internal elastic lamina with media thinning secondary to smooth muscle atrophy and frequent lack of atherosclerosis.[21]

Involvement of the BA may be more significant, as there may be a lack of compensatory flow from either vertebral artery to perfuse distal to the ectatic vessel.[19–21] The BA also perfuses the pontine penetrator arteries, which may become occluded at their origins by micro-emboli associated with turbulent blood flow in the dolichoectatic vessels.[20][21][24] Some investigators have assessed the radiological characteristics of BA dolichoectasia in association with posterior circulation infarcts, including the vertical height of the BA and the presence of concomitant atherosclerosis.[21] These characteristics, based on CT criteria, have not been prospectively validated or scientifically quantified, and do not take into account the other non-ischaemic complications of VBD, but they do give further support to the importance of BA involvement in PCD. Compression of the pons by an ectatic BA could potentially cause bilateral dysfunction, depending on its anatomical position, and a worse clinical presentation and prognosis than unilateral vertebral artery compression.

CONCLUSIONS

This study suggests that VBD may be a congenital, non-atherosclerotic vasculopathy and be independently associated with neurological morbidity and mortality in adult populations. The cumulative survival curve suggests that VBD confers a higher mortality rate than expected in affected individuals. Prospective large population studies are needed to elucidate the natural history of this vasculopathy and further delineate its clinical significance and underlying pathogenesis. There is an urgent need to develop and scientifically validate angiographic criteria for the radiological diagnosis of VBD in order to standardise the diagnosis and avoid under-reporting of this uncommon but clinically significant vasculopathy.

ACKNOWLEDGEMENTS

. . . .

Authors' affiliations

O O Zaidat, Duke University Medical Center, Department of Radiology, Durham, NC, USA

E E Ubogu, Department of Neurology, Emory University School of Medicine, Atlanta, GA, USA

REFERENCES

1 **Biller J**, Love BB. Ischemic cerebrovascular disease. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD, eds. *Neurology in clinical practice: the neurologic disorders*, 3rd ed, vol. 2. Boston: Butterworth and Heinemann, 2000:1125–66.
2 **Ubogu EE**, Chase CM, Verrees MA, *et al.* Cervicomedullary junction compression caused by vertebral artery dolichoectasia and requiring surgical treatment. Case report. *J Neurosurg* 2002;**96**:140–3.
3 **Carella A**, Caruso G, Lamberti P. Hemifacial spasm due to elongation and ectasia of the distal segment of the vertebral artery. Report of two cases. *Neuroradiology* 1973;**6**:233–6.
4 **de Oliveira R de M**, Cardeal JO, Lima JG. (Basilar ectasia and stroke: Clinical aspects of 21 cases.) 1997;**55**:558–62.
5 **Deeb ZL**, Jannetta PJ, Rosenbaum AE, *et al.* Tortuous vertebrobasilar arteries causing cranial nerve syndromes: Screening by computed tomography. *J Comput Assist Tomogr* 1979;**3**:774–8.
6 **Hongo K**, Nakagawa H, Morota N, *et al.* Vascular compression of the medulla oblongata by the vertebral artery: report of two cases. *Neurosurgery* 1999;**45**:907–10.
7 **Nuti D**, Passero S, Di Girolamo S. Bilateral vestibular loss in vertebrobasilar dolichoectasia. *J Vestib Res* 1996;**6**:85–91.
8 **Yu YL**, Moseley IF, Pullicino P, *et al.* The clinical picture of ectasia of the intracerebral arteries. *J Neurol Neurosurg Psychiatry* 1982;**45**:29–36.
9 **Himi T**, Kataura A, Tokuda S, *et al.* Downbeat nystagmus with compression of the medulla oblongata by dolichoectatic vertebral arteries. *Am J Otol* 1995;**16**:377–81.
10 **Kim P**, Ishijima B, Takahashi H, *et al.* Hemiparesis caused by vertebral artery compression of the medulla oblongata. Case report. *J Neurosurg* 1985;**62**:425–9.
11 **Maruyama K**, Tanaka M, Ikeda S, *et al.* (A case report of quadriparesis due to compression of the medulla oblongata by the elongated left vertebral artery.) *Rinsho Shinkeigaku* 1989;**29**:108–11.
12 **Milandre L**, Bonnefori B, Pestre P, *et al.* (Vertebrobasilar arterial dolichoectasia. Complications and prognosis.) *Reu Neurol (paris)* 1991;**147**:714–22.
13 **Vincentelli F**, Caruso G, Rabehanta PB, *et al.* Surgical treatment of a rare congenital anomaly of vertebral artery: Case report and review of the literature. *Neurosurgery* 1991;**28**:416–20.
14 **Milandre L**, Martini P, Perot S, *et al.* Pure motor hemiparesis in case of vertebrobasilar arterial ectasia. *Neuroradiology* 1993;**35**:196–8.
15 **Moss MS**, West RJ. Ectasia of the vertebral artery as a cause of isolated pyramidal tract signs: Case report and a review of literature. *Br J Neurosurg* 1996;**10**:497–9.
16 **Miyazaki M**, Hashimoto T, Sakurama N, *et al.* Central sleep apnea and arterial compression of the medulla. *Ann Neurol* 1991;**29**:564–5.
17 **Smoker WRK**, Corbett JJ, Gentry LR, *et al.* High-resolution computed tomography of the basilar artery. 2. Vertebrobasilar dolichoectasia: Clinical-pathologic correlation and review. *AJNR Am J Neuroradiol* 1986;**7**:61–72.
18 **Giang DW**, Perlin SJ, Monajati A, *et al.* Vertebrobasilar dolichoectasia: Assessment using MR. *Neuroradiology* 1988;**30**:518–23.
19 **Rautenberg W**, Aulich A, Rother J, *et al.* Stroke and dolichoectatic intracranial arteries. *Neurol Res* 1992;**14**(Suppl 2):201–3.
20 **Ince B**, Petty GW, Brown RD Jr, *et al.* Dolichoectasia of the intracranial arteries in patients with first ischemic stroke: a population-based study. *Neurology* 1998;**50**:1694–8.
21 **Passero S**, Filosomi G. Posterior circulation infarcts in patients with vertebrobasilar dolichoectasia. *Stroke* 1998;**29**:653–9.
22 **Samuels OB**, Joseph GJ, Lynn MJ, *et al.* A standardized method of measuring intracranial arterial stenosis. *AJNR Am J Neuroradiol* 2000;**21**:643–6.
23 **Rabb CH**, Barnwell SL. Catastrophic subarachnoid hemorrhage resulting from ruptured vertebrobasilar dolichoectasia: case report. *Neurosurg* 1998;**42**:379–82.
24 **De Georgia M**, Belden J, Pao L, *et al.* Thrombus in vertebrobasilar dolichoectatic artery treated with intravenous urokinase. *Cerebrovasc Dis* 1999;**9**:28–33.